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L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2000 ACS
AN 1998:618088 CAPLUS
DN 129:310286
TI The glycine site on the NMDA receptor: structure-activity relationships and possible therapeutic applications
AU Dannhardt, G.; Kohl, B. K.
CS Institute of Pharmacy, Johannes Gutenberg-University, Mainz, D-55099, Germany
SO Curr. Med. Chem. (1998), 5(4), 253-263
CODEN: CMCHE7; ISSN: 0929-8673
PB Bentham Science Publishers
DT Journal; General Review
LA English
AB A review with 58 refs. L-glutamate is the most important fast excitatory neurotransmitter in the mammalian central nervous system. Glutamate receptors are classified into two main categories: ionotropic and metabotropic. The N-methyl-D-aspartate (NMDA) receptor, which is assocd. with an ion channel, seems to play an important role in glutamate excitotoxicity, a process thought to be involved in a no. of neurodegenerative disorders such as focal cerebral **ischemia** (stroke), Parkinson's disease, Huntington's disease, Alzheimer's disease, schizophrenia and epilepsy. The unique glycine site on the NMDA receptor, discovered by Johnson and Ascher in 1987, represents an interesting target for the development of neuroprotective compds. Glycine antagonists may offer advantages over other NMDA antagonists in terms of their side-effect profile, esp. in the long-term treatment of chronical neurodegenerative disorders but also in the treatment of serious medical emergencies with a significant morbidity and mortality like status epilepticus or stroke. So far it is not clear whether NMDA receptor antagonists including glycine antagonists would be suitable for chronic administration because of their effects on cognition, learning and motor function. High-affinity, in vivo potent, glycine antagonists of great structural diversity (i. e. pyrido[2,3-b]pyrazine-N-oxides, indole-2-carboxylates, 4-substituted-3-phenylquinoline-2(1H)-ones and alkyl-substituted 1,4-dihydro-quinoxaline-2,3-diones) are now available and their suitability for long-term treatment of chronical neurodegenerative disorders has to be investigated in clin. trials.

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2000 ACS
AN 1995:964767 CAPLUS
DN 124:20673
TI **Glycine-site NMDA receptor antagonists**
AU Kulagowski, Janusz J; Leeson, Paul D
CS Neuroscience Research Centre, Merck Sharp & Dohme Research Laboratories, Harlow/Essex, CM20 2QR, UK
SO Expert Opin. Ther. Pat. (1995), Volume Date 1995, 5(10), 1061-75
CODEN: EOTPEG; ISSN: 1354-3776
DT Journal; General Review
LA English

AB A review with refs. The patent literature on antagonists for the glycine site of the NMDA receptor, covering the 2 yr prior to July 1995, is reviewed. Compd. classes reported include quinoxaline-2,3-diones; imidazolopyrazinones; triazolopyrimidones; pyridazinoquinolines; benz[b]azepine-2,5-diones; 1,2,4-benzothiadiazine-1,1-dioxides; 2-carboxyindoles; 2-quinolones; misc. other compds., and kynurenine-derived mols. Glycine site antagonists have an improved therapeutic index relative to other classes of NMDA antagonists, and show considerable therapeutic promise for CNS disorders, including cerebral **ischemia**, epilepsy, head injury and schizophrenia. Glycine site antagonists with useful in vivo activity are currently limited to the N-hydroxypyrrolidinones, R(+)-HA-966 and L-68,414; the quinoxaline-2,3-diones, ACEA 1021 and SM-18400; and the 4-hydroxy-2-quinolone, L-701,324.

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2000 ACS
AN 1995:448681 CAPLUS
DN 122:282059
TI **Glycine site NMDA receptor antagonists** provide protection against **ischemia**-induced neuronal damage in hippocampal slice cultures
AU Newell, D. W.; Barth, A.; Malouf, A. T.
CS Department of Neurological Surgery, University of Washington, School of Medicine, Seattle, WA, 98195, USA
SO Brain Res. (1995), 675(1,2), 38-44
CODEN: BRREAP; ISSN: 0006-8993
DT Journal
LA English
AB **Ischemia**-induced neuronal injury can be reduced by glutamate antagonists acting at the N-methyl-D-aspartate (NMDA) receptor. 7-Chlorokynurenic acid and the recently synthesized compd. Acea 1021 block NMDA receptors by acting at the strychnine-insensitive glycine site. The anti-ischemic properties of these compds. were tested by evaluating their ability to reduce CA1 neuronal damage in hippocampal slice cultures deprived of oxygen and glucose. Acea 1021 and 7-chlorokynurenic acid significantly reduced CA1 injury produced by oxygen and glucose deprivation in a dose-dependent manner. The neuroprotective effect of these compds. was reversed by the addn. of glycine. The phencyclidine site NMDA antagonist MK-801 also provided significant protection to CA1 neurons against the same insult, and this protection was not affected by the addn. of glycine. These results indicate that Acea 1021 and 7-chlorokynurenic acid can provide protection to CA1 neurons against **ischemia**-induced injury by a glycine-sensitive mechanism.

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FILE 'REGISTRY' ENTERED AT 08:39:50 ON 04 JAN 2000
E FELBAMATE/CN
L1 1 S E3

FILE 'CAPLUS' ENTERED AT 08:40:51 ON 04 JAN 2000
L2 11 S GLYCINE SITE NMDA RECEPTOR ANTAGONIST?
L3 38519 S ISCHEMIA OR EMBOLISM

L4 3 S L2 AND L3